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Risk Factors for Fatal Outcome From Rocky Mountain Spotted Fever in a Highly Endemic Area—Arizona, 2002–2011

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Abstract

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Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online (http://cid.oxfordjournals.org). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

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Background—Rocky Mountain spotted fever (RMSF) is a disease that now causes significant morbidity and mortality on several American Indian reservations in Arizona. Although the disease is treatable, reported RMSF case fatality rates from this region are high (7%) compared to the rest of the nation (<1%), suggesting a need to identify clinical points for intervention.

Methods—The first 205 cases from this region were reviewed and fatal RMSF cases were compared to nonfatal cases to determine clinical risk factors for fatal outcome.

Results—Doxycycline was initiated significantly later in fatal cases (median, day 7) than nonfatal cases (median, day 3), although both groups of case patients presented for care early (median, day 2). Multiple factors increased the risk of doxycycline delay and fatal outcome, such as early symptoms of nausea and diarrhea, history of alcoholism or chronic lung disease, and abnormal laboratory results such as elevated liver aminotransferases. Rash, history of tick bite, thrombocytopenia, and hyponatremia were often absent at initial presentation.

Conclusions—Earlier treatment with doxycycline can decrease morbidity and mortality from RMSF in this region. Recognition of risk factors associated with doxycycline delay and fatal outcome, such as early gastrointestinal symptoms and a history of alcoholism or chronic lung disease, may be useful in guiding early treatment decisions. Healthcare providers should have a low threshold for initiating doxycycline whenever treating febrile or potentially septic patients from tribal lands in Arizona, even if an alternative diagnosis seems more likely and classic findings of RMSF are absent.

Keywords

Rocky Mountain spotted fever; American Indians; tick-borne; fatalities; *Rhipicephalus sanguineus*

Rocky Mountain spotted fever (RMSF), caused by the tick-borne bacterium *Rickettsia rickettsii*, can be a rapidly fatal disease even in previously healthy people. Before the discovery of effective antibiotics, reported fatality ranged from approximately 20% to 80% [1]. Doxycycline is the recommended treatment for suspected RMSF, regardless of patient age, and other commonly used broad-spectrum antibiotics are not effective in preventing death [2–4]. When doxycycline treatment is started in the first 5 days of symptoms, fatal outcome is unlikely; however, treatment efficacy decreases sharply after day 5 of symptoms [4–6].RMSF is difficult to diagnose during the first days of illness because presenting symptoms are nonspecific and diagnostic testing lacks sensitivity during this time [7]. Therefore, to prevent fatalities, clinicians must treat empirically as soon as the disease is suspected [2].

RMSF was reported sporadically in Arizona until an outbreak investigation in 2003 identified a new vector for this disease in the United States, *Rhipicephalus sanguineus* [8]. Human cases were identified from as early as 2002 in one small community (community A), and molecular typing of the pathogen collected from human Arizona samples and *R. sanguineus* ticks confirmed *R. rickettsii* as the etiology of this outbreak [9, 10].

There have now been reports of cases from 6 tribal communities that have ecological conditions ranging from dry, hot desert to mountain pine forests [11]. The similarity

between affected communities is that all have free-roaming dogs with some degree of *R. sanguineus* infestation, as seen in the original investigation in community A [12].

Early, anecdotal reports from physicians in this region suggested differences in the epidemiology and clinical presentation of RMSF compared with other regions of the United States. An article published concurrently characterizes these differences, such as extended seasonality, younger age distribution, and lack of rash [13]. Another concerning difference was the high case fatality rate. Among 219 cases reported from tribal lands in Arizona from 2003 to 2011, 16 died (7.3%) [14]; in contrast, the reported case fatality rate elsewhere in the United States was <1% [15]. Although there are multiple factors that may contribute to underestimation of the US case fatality rate, the number of fatalities seen each year from these 2 small communities was concerning. At the request of local healthcare providers and the first 2 Arizona tribal communities affected, we reviewed medical records of the first 205 RMSF cases to assess risk factors for fatal outcome and identify clinical points of intervention to save lives.

METHODS

Data collection, healthcare facilities, and service populations have been described [13]. Approval for the study was obtained from participating tribes, the Indian Health Service, and the Centers for Disease Control and Prevention (CDC). The study was intended to prevent disease in response to an immediate public health threat and was therefore judged exempt by the CDC institutional review board on a nonresearch basis. The study was approved by the community A and B tribal councils through resolutions 11-2010-302 and AU-11-223, respectively. Cases included those diagnosed from 2002 through 30 September 2011. Case definitions and definitions of terms used in this manuscript are presented in the concurrent article by Traeger et al [13]. The following additional terms were used in this manuscript: Outpatient visit is a visit to the clinic or the emergency department, resulting in discharge home. Severe outcome includes any hospital admission (including intensive care unit [ICU] admission) or fatality. Late treatment is treatment with doxycycline initiated on day 5 of symptoms or later. A late symptom is a symptom that began on day 4 of illness or later. All diagnoses and causes of death were taken directly from the medical record.

Fatal cases were compared to nonfatal cases to identify risk factors for fatal outcome. Patients who received late treatment were compared to patients who were treated early (received doxycycline in the first 4 days of illness) to identify findings that may be risk factors for late treatment. If there was no information regarding a specific variable documented in the medical record, the case was not included in the analyses for that variable. Data were analyzed using EpiInfo [16]. Statistical differences in categorical variables were evaluated using the χ^2 test; when the expected value of a cell was <5, Fisher exact test was used. Statistical differences in continuous variables were evaluated using analysis of variance or the Mann–Whitney/Wilcoxon 2-sample test when a nonparametric test was more appropriate. Statistical significance was set at $\alpha = .05$.

RESULTS

Demographics and History

Among 205 cases of RMSF included in this analysis, 190 (93%) were nonfatal cases and 15 (7%) were fatal cases (Table 1). Among cases, 85 were confirmed and 120 met the probable RMSF case definition. Fourteen fatal cases and 1 nonfatal case were confirmed by polymerase chain reaction (PCR) at the CDC. Additional sequencing was performed on a subset of these samples [9]. All case patients except 1 were identified as American Indians. The mean age of all case patients was 20 years, and mean age did not significantly differ between fatal and nonfatal cases. Children aged ≤10 years comprised 101 of 190 (53%) nonfatal cases and 7 of 15 (47%) fatal cases (Supplementary Figure 1). The median number of deaths per year during this time period was 1.7 and ranged from a low of 0 deaths in 2007 to a high of 5 deaths in 2011.

The months with the highest proportion of fatal cases were April (25%), August (14%), and October (14%) (Supplementary Figure 2). Of the medical conditions collected, only a history of alcoholism (among adults) and chronic lung disease (CLD) were significant risk factors for fatal outcome, and only a history of alcoholism (risk ratio [RR], 1.84; 95% confidence interval [CI], 1.14–2.99) and CLD (RR, 2.88; 95% CI, 2.34–3.45) were significant risk factors for late treatment with doxycycline.

Symptoms

Fever (which included subjective reports) was the most common symptom (Table 2). All fatal cases included a fever during the course of illness, either subjective or measured. Whereas most of the symptoms that were more common in fatal cases occurred late in disease, gastrointestinal symptoms (abdominal pain, anorexia, nausea, vomiting, and diarrhea), hepatomegaly, splenomegaly, and peripheral edema typically began during the first 3 days of illness. Of the symptoms recorded, those significantly correlated with late treatment were headache (RR, 1.82; 95% CI, 1.10–3.02), nausea (RR, 1.72; 95% CI, 1.08–2.75), diarrhea (RR, 1.66; 95% CI, 1.08–2.55), periorbital edema (RR, 2.61; 95% CI, 1.67–4.07), dizziness (RR, 2.17; 95% CI, 1.22–3.84), and mental status change (RR, 2.66; 95% CI, 1.84–3.85). To provide a thorough clinical picture, frequencies of signs and symptoms were stratified by age (Supplementary Table 2B).

Rash occurred significantly later in fatal cases (median, day 5.5; range, 1–9) than in nonfatal cases (day 2; range, 1–14) (Table 3). Petechial rash was uncommon and late in disease course when present, occurring in 30 of 120 (15%) cases, on median day 7 of illness. A significantly higher proportion of fatal cases included a petechial rash with no evidence of prior maculopapular rash (6/12 [50%]) compared with 12 of 107 (11%) nonfatal cases in which the rash was described as petechial only.

Medical Care and Treatment

A median of 2 outpatient visits was recorded during both fatal and nonfatal cases, and both presented on day 2 of symptoms. However, the first notation of RMSF in the medical record occurred significantly later in fatal cases (median, day 7; range, 1–9) than nonfatal cases

(median, day 3; range, 1–14) (Table 3). The median day of symptoms that doxycycline was initiated was significantly later among fatal cases (day 7; range, 6–9) than nonfatal cases (day 3; range, 1–14). The median interval between the first notation of RMSF and initiation of doxycycline treatment was 0 days for both fatal and nonfatal cases.

None of the patients who died received doxycycline before day 6 of symptoms; however, most (52/62 [83.9%]) of the patients with documentation of late treatment survived. The following antibiotics were initiated within the first 3 days of symptom onset, but did not prevent death: ampicillin/sulbactam, ceftriaxone, clindamycin, cefazolin, gentamycin, vancomycin, imipenum, and amoxicillin. Azithromycin was administered to 2 case patients with confirmed RMSF, but mental status deterioration occurred in both and therapy was changed to doxycycline prior to day 6 of symptoms; both patients survived, but required ICU care for >7 days.

Laboratory Findings

Initial complete blood count, chemistry panel, and liver enzymes were performed later in fatal cases (Table 3). Abnormalities were more frequent in fatal cases for all laboratory results except gamma-glutamyl transpeptidase (Table 4). Laboratory abnormalities that were significantly correlated with late treatment with doxycycline included thrombocytopenia (RR, 1.98; 95% CI, 1.33–2.93), elevated AST (RR, 1.75; 95% CI, 1.10–2.78), elevated ALT (RR, 1.97; 95% CI, 1.31–2.95), and elevated total bilirubin (RR, 2.04; 95% CI, 1.35–3.09). An abnormal urine finding was more frequent in fatal than nonfatal cases (RR, 2.22; 95% CI, .66–7.40) (Supplementary Table 4B). There were 5 fatal cases and 17 nonfatal cases with ≥5 white blood cells in the first urine sample tested (RR, 2.22; 95% CI, .66–7.40).

Severe Outcomes

Eighty-six cases (42%) involved severe outcomes, including 15 fatalities and 71 hospitalizations. Patients treated early were more likely to be managed as outpatients (Table 5). However, the frequency of hospitalization and fatal outcome increased rapidly as the disease progressed without doxycycline treatment. There were 29 patients requiring admission to the ICU (Table 6). A majority of deaths (n = 13) occurred in the ICU, and 2 occurred in the emergency department. The median day of symptoms that death occurred was day 9 (range, 6–20) (Table 3), and the most common causes of death listed in the medical record were sepsis (n = 9), disseminated intravascular coagulation (DIC; n = 7), multisystem organ failure (n = 5), and acute respiratory distress syndrome (ARDS; n = 3).

There were wide variations in the clinical presentations of the 15 fatal cases. Three patients were afebrile when temperature was measured at the first visit, and 2 of these patients (a 2-year-old child and 39-year-old man) also had no history of subjective fever prior to presentation. The 39-year-old man did develop a measured fever after admission. However, the child had a subjective fever reported by the parent only and was afebrile whenever temperature was measured by the provider. Only 1 case patient who ultimately died was diagnosed with RMSF at the first visit, and treatment initiated at time of presentation on day 7 was not effective at preventing death.

DISCUSSION

This review of RMSF cases from 2 tribal communities in Arizona demonstrates the rapidly progressive nature of this disease and the need for early diagnosis and treatment. None of the fatal cases received early treatment with doxycycline. Treatment delay has often been linked to increased risk of fatal outcome [4–7, 17–19] and represents an important factor that is potentially modifiable in the clinical setting. Therefore, analysis was performed to determine which factors were associated with late treatment and may represent signals that should prompt early suspicion of the disease.

The prompt initiation of doxycycline treatment once RMSF was suspected in this patient cohort demonstrates that local providers are highly aware of appropriate antibiotic choice for RMSF. In this patient population, like others in the United States [6], patients with RMSF presented to healthcare providers early and returned multiple times. The first notation of RMSF in the medical records was late in fatal cases (median day 7), suggesting that the problem lies in the provider's initial delay to include RMSF in the differential diagnosis for some patients. This case review identifies multiple factors that both complicate the initial presentation of RMSF and, at times, make another diagnosis appear more likely. Understanding of these factors may improve early recognition of RMSF and decrease morbidity and mortality from this disease.

Patients with a medical history of CLD or alcoholism were at greater risk of both receiving doxycycline late and dying of the disease. It is unclear if the small number of patients with CLD identified in this review represents a true significant risk factor; however, a history of alcoholism is likely to be significant. A higher risk of fatal outcome from other rickettsial diseases in patients with a history of alcoholism has been reported [20]. In this study, altered mental status, elevated aminotransferases, and low platelets were all found to be significantly correlated with late treatment, and the medical records suggested that providers sometimes attributed these signs and symptoms to complications of alcoholism in patients with this history. Altered mental status frequently occurs with alcohol intoxication, and elevated liver aminotransferases and low platelet counts are common sequelae of alcohol-related liver disease. Also, patients with a history of alcoholism are at higher risk for other severe febrile illnesses, such as aspiration pneumonia, that may seem more likely than RMSF [21]. These factors, in addition to incomplete history of present illness provided by acutely intoxicated patients, may lead to delayed diagnosis, delayed treatment, and a higher risk of fatal outcome in these patients. Providers in the region should consider doxycycline early in febrile patients with a history of alcoholism, even if an alternative diagnosis seems more likely.

Other factors that may complicate presentation include abdominal symptoms, such as nausea and diarrhea, and abnormal urine findings. Abdominal pain is a symptom of RMSF that has led to misdiagnosis in other published reports [22, 23]. Diarrhea, often seen as an indicator of a benign process, such as viral gastroenteritis, was significantly correlated with late treatment and death in this study. Primary abdominal complaints led to 1 initial diagnosis of acute gastroenteritis and 2 diagnoses of nonspecific abdominal pain in fatal cases. In this review, the occurrence of abdominal pain, pyuria, and fever were initially diagnosed as

pyelonephritis and resulted in delayed diagnosis of RMSF and death in 2 patients. Even in the presence of abnormal urine findings or diarrhea, abdominal symptoms should be considered important early clinical triggers to initiate doxycycline in patients from this region.

While the factors described above may contribute to a complicated presentation of RMSF when present, there are additional factors that complicate by their absence. Rash appeared late in fatal cases (median, day 5.5 of symptoms), and this has been a documented risk factor for fatal outcome in other studies [24, 25]. In addition, although all fatal cases included fever, some patients were afebrile when temperature was measured at first presentation, and subjective reports of fever should not be discounted. Abnormal laboratory findings were more likely to be seen later as the disease progressed untreated. Relying on the presence of a rash, clinically measured fever, or laboratory abnormalities may lead to missed opportunities to begin treatment at the first visit.

This review is subject to several limitations. Patients with titers <1:128 or with enzyme-linked immunosorbent assay testing alone are included in the national case definition for reporting, but were excluded from this analysis to improve the stringency of our findings. Furthermore, the higher case fatality rate seen in this region may be influenced by active testing of fatal cases through PCR confirmation at the CDC, a practice rarely pursued elsewhere [18, 26]. Thus, the rate calculated through national surveillance may be low due to national underreporting of fatalities and overinclusion of nonfatal cases that may not be true RMSF. Also, serologic testing lacks the specificity to differentiate between other spotted fever group rickettsia (SFGR); however, when PCR testing has been performed on samples from ill humans from these 2 communities, *R. rickettsia* has been the only SFGR detected. Finally, this study is a retrospective medical records review, and cases were managed and documented at the time of illness by physicians with no knowledge of this study, or that these records would be reviewed. The diagnoses and causes of death were taken from what the physician documented in the actual medical record, and the exact clinical criteria used to make diagnoses such as ARDS, DIC, renal failure, etc, might have varied between physicians.

Since the initial discovery of RMSF in this region, a high level of knowledge among providers has developed, as evidenced by high rates of doxycycline prescription among cases when RMSF is suspected; however, progress remains to be made. Improving early consideration of RMSF in patients with complicated presentations, such as those with history of alcoholism or signs and symptoms of another illness, and for those without classic signs and symptoms of RMSF, such as rash, will reduce mortality.

Changes in clinical practice should be encouraged through targeted provider education and healthcare facility oversight for local providers, and those at tertiary care facilities receiving transferred tribal patients, to ensure proper treatment is continued and confirmatory testing is completed. The treatment for RMSF, a short course of doxycycline, should be used even when the likelihood of RMSF seems low, to prevent fatalities similar to the ones that occurred in this population. The dose and duration of doxycycline used for RMSF have not

been shown to stain permanent teeth when given to pediatric patients [27], and doxycycline should be prescribed regardless of patient age based on clinical suspicion alone.

A clinical description of these RMSF case patients, with a comparison to patients who presented with similar febrile illnesses, is published concurrently [13]. Finally, public health interventions such as animal control, vector control, and veterinary care are essential to reduce overall incidence and mortality from RMSF. Cost analysis of medical care and loss of life and productivity caused by RMSF in this region may be helpful in illustrating that prevention measures are not only lifesaving, but cost effective.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Demographics, Exposures, and Medical History Reported for Fatal and Nonfatal Cases of Rocky Mountain Spotted Fever in 2 Tribal Communities in Eastern Arizona

Demographics	All Cases, No. (%)	Nonfatal, No. (%)	Fatal Cases	RR	95% CI
No. of cases	205	190/205 (93)	15/205 (7)		
Mean age	19.8	19.5	23.7		P =.43[a]
Child (<18 y)	123/205	115/123 (94)	8/123 (7)	0.76	.29–2.02
Male sex	106/205 (51.7)	95/190 (50)	11/15 (73.3)	2.56	.85–7.80
Exposures					
Tick exposure	73/132 (55)	71/125 (57)	2/7 (29)	0.32	.07–1.61
Tick bite	36/125 (29)	34/118 (29)	2/7 (29)	0.99	.18–5.34
Dog contact	77/90 (85.6)	72/85 (84.7)	5/5 (100)	Undefined	Undefined
Sick contacts	17/43 (40)	15/36 (42)	2/5 (29)	0.61	.13–2.80
Travel	6/37 (16)	6/31 (19)	0/6 (0)	0	Undefined
Medical history					
Autoimmune disease	2/205 (1.0)	2/190 (1.1)	0/15 (0)	0	Undefined
Tuberculosis	2/204 (1.0)	2/189 (1.1)	0/15 (0)	0	Undefined
Asthma	17/205 (8.3)	16/190 (8.4)	1/15 (6.7)	0.79	.11–5.65
Chronic lung disease	4/205 (2)	1/190 (0.5)	3/15 (20.0)	12.56	5.71–27.63
Heart disease	4/205 (2.0)	3/190 (1.6)	1/15 (6.7)	3.59	.61–21.09
Hypertension	26/205 (12.7)	24/190 (12.6)	2/15 (13.3)	1.06	.25–4.43
Diabetes	18/204 (8.8)	18/189 (9.5)	0/15 (0)	0	Undefined
Thyroid disease	6/205 (2.9)	6/190 (3.2)	0/15 (0)	0	Undefined
Hepatitis	3/204 (1.5)	3/189 (1.6)	0/15 (0)	0	Undefined
Alcoholism[b]	22/81 (27.2)	16/74 (21.6)	6/7 (85.7)	16.09	2.05–126.20

The following conditions did not occur in any patients in this study: AIDS/HIV, history of solid organ or bone marrow transplant, asplenia, G6PD, or history of renal insufficiency/failure. The following conditions only occurred in 1 nonfatal case each, and no fatal cases: immune compromise, cancer, stroke, deep vein thrombosis, and sickle cell disease.

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; RR, risk ratio.

[a] Analysis of variance.

[b] Analysis for alcoholism included only cases aged >17 years.

Table 2

Signs and Symptoms Reported for Fatal and Nonfatal Cases of Rocky Mountain Spotted Fever in 2 Tribal Communities in Eastern Arizona

Symptom	Day of Onset, Median (Range)	Nonfatal Frequencies, No. (%)	Fatal Frequencies, No. (%)	RR	95% CI
Fever	Day 1 (1–14)	149/187 (79.7)	15/15 (100)	Undefined	Undefined
T_{max}, median		101.8 (96.4–106.3)	103.2 (100.4–105.7)	*P* =.01	
Chills	Day 1 (1–14)	43/123 (35)	4/10 (40)	1.22	.36–4.11
Headache	Day 1 (1–14)	72/126 (57.1)	6/9 (66.7)	1.46	.38–5.60
Rash	Day 2 (1–14)	117/178 (65.7)	13/14 (92.9)	6.20	.83–46.34
Abdominal pain	Day 3 (1–9)	41/145 (28.3)	7/9 (77.8)	7.73	1.67–35.84
Anorexia	Day 1.5 (1–9)	43/116 (37.1)	8/9 (88.9)	11.61	1.50–89.99
Nausea	Day 1 (1–9)	65/146 (44.5)	9/10 (90)	9.97	1.29–76.85
Vomiting	Day 1 (1–10)	68/157 (43.3)	9/12 (75)	3.58	1.01–12.78
Diarrhea	Day 1 (1–8)	44/151 (29.1)	8/12 (67)	4.27	1.35–13.54
Hepatomegaly	Day 3 (1–11)	5/135 (3.7)	2/10 (20)	4.93	1.28–19.02
Splenomegaly	Day 1.5 (0–7)	1/133 (0.8)	1/10 (10)	7.83	1.71–35.93
Coughing	Day 1 (1–12)	62/157 (39.5)	6/12 (50)	1.49	.50–4.41
Wheezing	Day 2 (1–6)	9/152 (5.9)	0/12 (0)	Undefined	Undefined
Chest pain	Day 1 (1–12)	10/118 (8.5)	2/11 (18.2)	2.17	.53–8.90
Nasal congestion	Day 1 (1–11)	40/145 (27.6)	3/10 (30.0)	1.12	.30–4.12
Sore throat	Day 1.5 (1–13)	26/126 (20.6)	1/8 (12.5)	0.57	.07–4.41
Difficulty swallowing	Day 2 (1–4)	2/112 (1.8)	1/8 (12.5)	5.57	.96–32.19
Ear pain	Day 3 (1–7)	12/118 (10.2)	1/8 (12.5)	1.24	.17–9.31
Conjunctivitis	Day 2 (1–10)	19/137 (13.9)	3/11 (27.3)	2.15	.62–7.48
Periorbital edema	Day 4 (1–9)	3/134 (2.2)	4/13 (30.8)	8.89	3.61–21.88
Photophobia	Day 1 (1–6)	5/109 (4.6)	0/8 (0)	0	Undefined
Fatigue	Day 2 (1–12)	51/118 (43.2)	9/12 (75)	3.5	.99–12.34
Lethargy	Day 5 (1–8)	17/111 (15.3)	7/10 (70.0)	9.43	2.63
Irritability	Day 3 (1–9)	17/114 (14.9)	3/9 (33.3)	2.58	.70–9.45
Dizziness	Day 1 (1–12)	19/103 (18.4)	2/7 (28.6)	1.7	.35–8.14

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Symptom	Day of Onset, Median (Range)	Nonfatal Frequencies, No. (%)	Fatal Frequencies, No. (%)	RR	95% CI
Neck pain	Day 5 (1–10)	16/132 (12.1)	0/9 (0)	0	Undefined
Seizures	Day 6 (1–10)	4/132 (3.0)	3/10 (30.0)	8.27	2.70–25.31
MSC	Day 5 (1–13)	16/155 (10.3)	13/14 (92.9)	62.76	8.54–461.09
Muscle pain	Day 1 (1–10)	50/118 (42.4)	3/11 (27.3)	0.54	.15–1.93
Peripheral edema	Day 3 (1–10)	13/133 (9.8)	5/14 (35.7)	3.98	1.50–10.56
LAD	Day 2.5 (1–9)	5/117 (4.3)	0/12 (0)	Undefined	Undefined
Jaundice	Day 4 (1–8)	2/135 (1.5)	4/14 (28.6)	9.53	4.19–21.71

Abbreviations: CI, confidence interval; LAD, lymphadenopathy; MSC, mental status change; RR, risk ratio; T_{max}, maximum recorded temperature during course of illness.

Table 3

Day of Notable Clinical Events for Fatal and Nonfatal Cases of Rocky Mountain Spotted Fever in 2 Tribal Communities in Eastern Arizona

Event	All Cases	Nonfatal	Fatal	*P* Value
Day of symptoms of first doctor visit	Day 2 (1–11)	Day 2 (1–11)	Day 2 (1–7)	
Day of symptoms that RMSF was first mentioned in medical record	Day 3 (1–14)	Day 3 (1–14)	Day 7 (1–9)	.005
Day of symptoms that doxycycline was started	Day 3 (1–14)	Day 3 (1–14)	Day 7 (6–9)	.000
Duration between first mention and treatment	0 days (0–10)	0 days (0–10)	0 days (0–5)	
Day of symptoms hospitalization occurred	Day 5 (1–11)	Day 4 (1–11)	Day 5 (1–9)	
Day of symptoms first CBC was obtained	Day 3 (1–14)	Day 3 (1–14)	Day 5.5 (1–9)	.008
Day of symptoms sodium was first tested	Day 3 (1–12)	Day 3 (1–12)	Day 5 (1–9)	.017
Day of symptoms AST was first tested	Day 3 (1–14)	Day 3 (1–14)	Day 7 (1–9)	.006
Day of symptoms that death occurred	NA	NA	Day 9 (6–20)	

Data are presented as median (range).

Abbreviations: AST, aspartate aminotransferase; CBC, complete blood count; NA, not applicable; RMSF, Rocky Mountain spotted fever.

Table 4

Abnormal Laboratory Findings for Fatal and Nonfatal Cases of Rocky Mountain Spotted Fever in 2 Tribal Communities in Eastern Arizona

	Nonfatal		Fatal			
Laboratory Parameter	**No. (%)**	**Day Test First Abnormal, Median (Range)**	**No. (%)**	**Day Test First Abnormal, Median (Range)**	**RR**	**95% CI**
Platelets (<130)	34/160 (21.3)	Day 5 (2–9)	14/15 (93.3)	Day 5.5 (2–9)	37.04	5.01–274.09
Sodium (<137)	64/158 (40.5)	Day 4 (1–12)	14/15 (93.3)	Day 6 (1–9)	17.05	2.29–126.82
AST (elevated)	73/148 (49.3)	Day 4 (1–14)	15/15 (100)	Day 7 (1–9)	Undefined	Undefined
ALT (elevated)	44/147 (29.9)	Day 4.5 (1–12)	12/15 (80.0)	Day 7 (1–9)	7.57	2.23–25.72
ALP (elevated)	80/146 (54.8)	Day 4 (1–14)	13/15 (86.7)	Day 6.5 (1–9)	4.75	1.11–20.37
GGT (elevated)	7/25 (28.0)	Day 6.5 (3–14)	2/4 (50.0)	Day 6.5 (6–7)	2.22	.37–13.38
Total bilirubin (elevated)	15/130 (11.5)	Day 5.5 (1–12)	10/13 (76.9)	Day 7 (2–9)	15.73	4.66–53.08

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; GGT, gamma-glutamyl transferase; RR, risk ratio.

Table 5

Outcome by Day of Symptoms That Treatment With Doxycycline Was Started for First 9 Days of Symptoms for Confirmed Cases of Rocky Mountain Spotted Fever in 2 Tribal Communities in Eastern Arizona

Day of Symptoms Treatment Was Started (Total No. of Confirmed Patients Treated on That Day)	Outpatient	Hospitalized	Subset of Hospitalized	Subset of Hospitalized and ICU
			ICU	Fatal
Day 1 (6)	5 (83)	1 (17)	0 (0)	0 (0)
Day 2 (11)	8 (73)	3 (27)	0 (0)	0 (0)
Day 3 (9)	4 (44)	5 (56)	1 (11)	0 (0)
Day 4 (7)	3 (43)	4 (57)	1 (14)	0 (0)
Day 5 (8)	2 (25)	6 (75)	4 (50)	0 (0)
Day 6 (9)	0 (0)	9 (100)	5 (55)	3 (33)
Day 7 (11)	0 (0)	11 (100)	4 (36)	3 (27)
Day 8 (5)	1 (20)	4 (80)	2 (40)	2 (40)
Day 9 (4)	0 (0)	4 (100)	4 (100)	2 (50)

Data are presented as No. (%).

Abbreviation: ICU, intensive care unit.

Table 6

Interventions and Notable Sequelae in Fatal and Nonfatal Cases of Rocky Mountain Spotted Fever in 2 Tribal Communities in Eastern Arizona

Intervention	Nonfatal, No. (%)	Fatal, No. (%)	RR	95% CI
ICU admission	16/189 (8.5)	13/15 (86.7)	39.22	9.33–164.88
Plasma transfusion	4/186 (2.2)	9/13 (69.2)	32.19	11.44–90.62
Platelet transfusion	5/186 (2.7)	10/12 (83.3)	61	14.69–253.38
PRBC transfusion	5/185 (2.7)	6/12 (50.0)	16.91	6.51–43.91
Whole blood transfusion	4/186 (2.2)	1/12 (8.3)	3.51	.55–22.20
Fluid boluses	77/186 (41.4)	14/14 (100)	Undefined	Undefined
Ventilation	6/189 (3.2)	15/15 (100)	Undefined	Undefined
Inotropic support	7/189 (3.7)	15/15 (100)	Undefined	Undefined
Immunoglobulins	0/184 (0)	1/12 (8.3)	17.73	9.98–31.47
ARDS	5/189 (2.6)	8/15 (53.3)	16.79	7.22–39.07
Respiratory failure	7/189 (3.7)	15/15 (100)	Undefined	Undefined
DIC	5/189 (2.6)	13/15 (86.7)	67.17	16.43–274.54
Multisystem organ failure	2/189 (1.1)	12/15 (80.0)	54.29	17.31–170.22
Renal insufficiency	7/189 (3.7)	10/14 (71.4)	27.35	9.59–78.00
Coma	2/188 (1.1)	9/15 (60)	26.18	11.36–60.37
Digital necrosis	1/186 (0.5)	2/15 (13.3)	10.15	3.90–26.45

Abbreviations: ARDS, acute respiratory distress syndrome; CI, confidence interval; DIC, disseminated intravascular coagulation; ICU, intensive care unit; PRBC, packed red blood cell; RR, risk ratio.